

We claim:

1. An isolated human antibody that specifically binds interleukin-1 receptor type 1 (IL-1R1), comprising a heavy chain and a light chain, wherein the heavy chain comprises a heavy chain variable region comprising an amino acid sequence as set forth in any of SEQ ID NO: 10, SEQ ID NO: 14, or SEQ ID NO: 16, or an antigen-binding or an immunologically functional immunoglobulin fragment thereof.
2. An isolated human antibody that specifically binds interleukin-1 receptor type 1 (IL-1R1), comprising a heavy chain and a light chain, wherein the light chain comprises a light chain variable region comprising an amino acid sequence as set forth in any of SEQ ID NO: 12 or SEQ ID NO: 18, or an antigen-binding or an immunologically functional immunoglobulin fragment thereof.
3. An isolated human antibody that specifically binds interleukin-1 receptor type 1 (IL-1R1), comprising a heavy chain and a light chain, wherein the heavy chain comprises an amino acid sequence as set forth in any of SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, or SEQ ID NO: 36, or an antigen-binding or an immunologically functional immunoglobulin fragment thereof.
4. An isolated human antibody that specifically binds interleukin-1 receptor type 1 (IL-1R1), comprising a heavy chain and a light chain, wherein the light chain comprises an amino acid sequence as set forth in any of SEQ ID NO: 38 or SEQ ID NO: 40, or an antigen-binding or an immunologically functional immunoglobulin fragment thereof.
5. An isolated human antibody that specifically binds interleukin-1 receptor type 1 (IL-1R1), wherein the antibody comprises:
 - a. a heavy chain having a heavy chain variable region comprising an amino acid sequence as set forth in SEQ ID NO: 10, an antigen-binding fragment

thereof, or an immunologically functional immunoglobulin fragment thereof, and a light chain having a light chain variable region comprising an amino acid sequence as set forth in SEQ ID NO: 12, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof;

5 b. a heavy chain having a heavy chain variable region comprising an amino acid sequence as set forth in SEQ ID NO: 14, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and a light chain having a light chain variable region comprising

10 an amino acid sequence as set forth in SEQ ID NO: 12, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof; or

15 c. a heavy chain having a heavy chain variable region comprising an amino acid sequence as set forth in SEQ ID NO: 16, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and a light chain having a light chain variable region comprising an amino acid sequence as set forth in SEQ ID NO: 18, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.

20 6. The antibody of claim 5, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 10, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain variable region having an amino acid sequence as set forth in SEQ ID NO: 12, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.

25 7. The antibody of claim 6, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO: 10, and wherein the light chain variable region comprises an amino acid sequence that has at least 90%

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sequence identity to the amino acid sequence as set forth in SEQ ID NO: 12, and wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).

8. The antibody of claim 5, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 14, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain variable region having an amino acid sequence as set forth in SEQ ID NO: 12, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
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9. The antibody of claim 8, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 14, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 12, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
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10. The antibody of claim 5, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 16, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain variable region having an amino acid sequence as set forth in SEQ ID NO: 18, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
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11. The antibody of claim 10, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 16, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 18,

wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).

12. An isolated human antibody that specifically binds interleukin-1 receptor type 1 (IL-1R1), wherein the antibody comprises:
 - 5 a. a light chain comprising an amino acid sequence as set forth in SEQ ID NO: 38, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof; and
 - b. a heavy chain comprising an amino acid sequence as set forth in SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 10 28, or SEQ ID NO: 30, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
13. The antibody of claim 12, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 20, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain variable region having an amino acid sequence as set forth in SEQ ID NO: 38, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
14. The antibody of claim 13, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 20, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 38, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
- 20 15. The antibody of claim 12, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 22, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain

- variable region having an amino acid sequence as set forth in SEQ ID NO: 38, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
16. The antibody of claim 15, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 22, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 38, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
17. The antibody of claim 12, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 24, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain variable region having an amino acid sequence as set forth in SEQ ID NO: 38, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
18. The antibody of claim 17, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 24, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 38, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
19. The antibody of claim 12, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 26, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain variable region having an amino acid sequence as set forth in SEQ ID NO: 38,

an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.

20. The antibody of claim 19, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 26, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 38, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
- 10 21. The antibody of claim 12, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 28, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain variable region having an amino acid sequence as set forth in SEQ ID NO: 38, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
- 15 22. The antibody of claim 21, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 28, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 38, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
- 20 23. The antibody of claim 12, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 30, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain variable region having an amino acid sequence as set forth in SEQ ID NO: 38, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
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24. The antibody of claim 23, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 30, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 38, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
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25. An isolated human antibody that specifically binds interleukin-1 receptor type 1 (IL-1R1), wherein the antibody comprises:
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- a. a light chain comprising an amino acid sequence as set forth in SEQ ID NO: 40, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof; and
 - b. a heavy chain comprising an amino acid sequence as set forth in SEQ ID NO: 32, SEQ ID NO: 34, or SEQ ID NO: 36, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
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26. The antibody of claim 25, wherein the heavy chain comprises a heavy chain variable region having an amino acid sequence as set forth in SEQ ID NO: 32, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises a light chain variable region having an amino acid sequence as set forth in SEQ ID NO: 40, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
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27. The antibody of claim 26, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 32, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 40, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
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28. The antibody of claim 25, wherein the heavy chain comprises an amino acid sequence as set forth in SEQ ID NO: 34, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises an amino acid sequence as set forth in SEQ ID NO: 40, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
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29. The antibody of claim 28, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 34, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 40, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
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30. The antibody of claim 25, wherein the heavy chain comprises an amino acid sequence as set forth in SEQ ID NO: 36, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof, and the light chain comprises an amino acid sequence as set forth in SEQ ID NO: 40, an antigen-binding fragment thereof, or an immunologically functional immunoglobulin fragment thereof.
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31. The antibody of claim 30, wherein the heavy chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 36, and wherein the light chain variable region comprises an amino acid sequence that has at least 90% sequence identity to the amino acid sequence as set forth in SEQ ID NO: 40, wherein the antibody specifically binds to an interleukin-1 receptor type 1 (IL-1R1).
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32. The antibody of claim 1, 2, 3, 4, 5, 12, or 25, wherein the heavy chain and light chain are connected by a flexible linker to form a single-chain antibody.
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33. The antibody of claim 32, which is a single-chain Fv antibody.

34. The antibody of claim 1, 2, 3, 4, 5, 12, or 25, which is a Fab antibody fragment.
35. The antibody of claim 1, 2, 3, 4, 5, 12, or 25, which is Fab' antibody fragment.
36. The antibody of claim 1, 2, 3, 4, 5, 12, or 25, which is a (Fab')₂ antibody fragment.
- 5 37. The antibody of claim 1, 2, 3, 4, 5, 12, or 25, wherein the antibody is a fully human antibody.
38. The antibody of claim 1, 2, 3, 4, 5, 12, or 25, wherein the antibody inhibits binding of IL-1 to its receptor.
- 10 39. A method of treating an IL-1 mediated disease in a patient, comprising administering to a patient a pharmaceutically effective amount of the antibody of claim 38.
40. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of the antibody of claim 38.
- 15 41. A method of treating an IL-1 mediated disease in a patient, comprising administering to a patient the pharmaceutical composition of claim 40.
42. A heavy chain comprising a variable region and a constant region, wherein the variable region comprises an amino acid sequence as set forth in any of SEQ ID NO: 10, SEQ ID NO: 14, or SEQ ID NO: 16, or an antigen-binding or an immunologically functional immunoglobulin fragment thereof.
- 20 43. A heavy chain comprising an amino acid sequence as set forth in any of SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34 or SEQ ID NO: 36, or an antigen-binding or an immunologically functional immunoglobulin fragment thereof.
- 25 44. A light chain comprising a variable region and a constant region, wherein the variable region comprises an amino acid sequence as set forth in any of SEQ

ID NO: 12 or SEQ ID NO: 18, or an antigen-binding or an immunologically functional immunoglobulin fragment thereof.

45. A light chain comprising an amino acid sequence as set forth in any of SEQ ID NO: 38 or SEQ ID NO: 40, or an antigen-binding or an immunologically functional immunoglobulin fragment thereof.

5 46. An isolated human antibody comprising:

a. human heavy chain framework regions, a human heavy chain CDR1 region, a human heavy chain CDR2 region, and a human heavy chain CDR3 region, wherein the human heavy chain CDR3 region has the amino acid sequence of SEQ ID NO: 67, SEQ ID NO: 68, or SEQ ID NO: 69; and

b. human light chain framework regions, a human light chain CDR1 region, a human light chain CDR2 region, and a human light chain CDR3 region, wherein the human light chain CDR3 region has the amino acid sequence of SEQ ID NO: 74 or SEQ ID NO: 75;

10 15 wherein the antibody specifically binds to interleukin-1 receptor type 1 (IL-1R1).

47. The isolated human antibody of claim 46, wherein the human heavy chain CDR2 region has the amino acid sequence of SEQ ID NO: 64, SEQ ID NO: 65, or SEQ ID NO: 66 and the human light chain CDR2 region has the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 73.

20 25 48. The isolated human antibody of claim 46, wherein the human heavy chain CDR1 region has the amino acid sequence of SEQ ID NO: 61, SEQ ID NO: 62, or SEQ ID NO: 63 and the human light chain CDR1 region has the amino acid sequence of SEQ ID NO: 70 or SEQ ID NO: 71.

49. An isolated human antibody comprising a human heavy chain CDR1 region, wherein the heavy chain CDR1 has the amino acid sequence of SEQ ID NO: 61, SEQ ID NO: 62, or SEQ ID NO: 63, and wherein the antibody specifically binds to interleukin-1 receptor type 1 (IL-1R1).

50. An isolated human antibody comprising a human heavy chain CDR2 region, wherein the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 64, SEQ ID NO: 65, or SEQ ID NO: 66, and wherein the antibody specifically binds to interleukin-1 receptor type 1 (IL-1R1).
- 5 51. An isolated human antibody comprising a human heavy chain CDR3 region, wherein the heavy chain CDR3 has the amino acid sequence of SEQ ID NO: 67, SEQ ID NO: 68, or SEQ ID NO: 69, and wherein the antibody specifically binds to interleukin-1 receptor type 1 (IL-1R1).
- 10 52. An isolated human antibody comprising a human light chain CDR1 region, wherein the light chain CDR1 has the amino acid sequence of SEQ ID NO: 70 or SEQ ID NO: 71, and wherein the antibody specifically binds to interleukin-1 receptor type 1 (IL-1R1).
- 15 53. An isolated human antibody comprising a human heavy chain CDR2 region, wherein the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 73, and wherein the antibody specifically binds to interleukin-1 receptor type 1 (IL-1R1).
- 20 54. An isolated human antibody comprising a human heavy chain CDR3 region, wherein the heavy chain CDR3 has the amino acid sequence of SEQ ID NO: 74 or SEQ ID NO: 75, and wherein the antibody specifically binds to interleukin-1 receptor type 1 (IL-1R1).
55. An isolated human antibody that specifically binds to the polypeptide of SEQ ID NO: 76.
56. The antibody of claim 55, wherein the antibody specifically binds Epitope 4 of IL1-R1.
- 25 57. The antibody of claim 5, 12, or 25, which is an IgG2 antibody.
58. The antibody of claim 5, 12, or 25, which binds specifically to the polypeptide of SEQ ID NO: 76.
59. The antibody of claim 5, 12, or 25, which binds specifically to Epitope 4 of IL-1R1.

60. A method for epitope mapping of a selected antigen, comprising:
- (a) generating a set of fusion proteins, wherein each fusion protein comprises
 - (i) avidin and (ii) a fragment of the antigen;
 - (b) screening the set of fusion proteins for binding to one or more specific binding partners for the antigen;
 - (c) isolating the fusion proteins on a medium comprising biotin, whereby the avidin binds to the biotin; and
 - (d) analyzing the fusion proteins bound by the specific binding partner or partners to determine binding sites on the antigen for the specific binding partner or partners.
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61. The method of claim 60, wherein the specific binding partners are antibodies.